## REMARKS

The specification and claims have been amended to include SEQ ID numbers which were omitted at the time of filing and correct erroneously numbered sequences. It has also been amended to include claiming priority statement under 35 U.S.C. § 119 (e).

Attached hereto is a marked version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

The undersigned hereby states that the paper copy of the substitute Sequence Listing and the computer readable form copy of the substitute Sequence Listing, submitted in accordance with 37 C.F.R. § 1.825(a) and (b), respectively, are the same and contain no new matter. Accordingly, entry of the substitute Sequence Listing into the above-captioned application is respectfully requested.

In the unlikely event that the patent office determines that extensions and/or other relief is required, applicant petition for any required relief including extensions of time and authorize the assistant commissioner to charge the cost of such petitions and/or fees due to our deposit account no. 03-1952 under order no. 532212000200. The assistant commissioner is not authorized to charge the cost of the issue fee to the deposit account.

Respectfully submitted,

April 11, 2002 By: _____

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Specification:**

Page 1, below the Title and above the Technical Field, has been amended as follows:

This application claims priority to US Patent application Ser. No.:53221-30002.00, filed August 10, 2000.

The paragraph, beginning at page1, line 8, has been amended as follows:

The present invention relates to the novel method for treating a patient that has osteoporosis and the patient may be having administered cyclase activating parathyroid hormone (CAP) or analogues. The patient receives an administration of a cyclase inhibiting parathyroid hormone peptide (CIP) having an amino acid sequence from between [(SEQ ID NO:1)] $PTH_{2-84}$ (SEQ ID NO:1) and [(SEQ ID NO:2)] $PTH_{34-84}$ (SEQ ID NO:3), preferably [(SEQ ID NO:3)] $PTH_{3-84}$ (SEQ ID NO:2) and [(SEQ ID NO:4)] $PTH_{28-84}$ (SEQ ID NO:8), or a conservatively substituted variant thereof exhibiting parathyroid hormone (PTH) antagonist activity in a therapeutically effective, but non-toxic amount that reduces the occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP, and yet, through a CAP rebound effect, it effective in itself in the treatment of osteoporosis.

The paragraph, beginning at page 2, line 1, has been amended as follows:

The complete or whole form of human PTH, (hPTH), is a unique 84 amino acid peptide (SEQ ID NO:5), as is shown in FIGURE 1. Researchers have found that this peptide has an anabolic effect on bone that involves a domain for protein kinase C activation (amino acid residues 28 to 34) as well as a domain for adenylate cyclase activation (amino acid residues 1 to 7). However, various catabolic forms of clipped or fragmented PTH peptides are also found in circulation, most likely formed by intraglandular or peripheral metabolism. For example, hPTH can be cleaved between amino acids 34 and 35 to produce a (1-34) PTH N-terminal fragment (SEQ ID NO:6) and a (35-84) PTH C-terminal fragment (SEQ ID NO:7). Likewise, clipping can

occur between either amino acids 36 and 37 or 37 and 38. Recently, a large PTH fragment referred to as "non-(1-84) PTH" has been disclosed which is clipped closer to the N-terminal end of PTH. (see R. LePage et *alia, "A non-(1-84) circulating parathyroid hormone (PTH) fragment interferes significantly with intact PTH commercial assay measurements in uremic samples"* Clin Chem (1998); 44:805-810).

The paragraph, beginning at page 4, line 16, has been amended as follows:

The present invention relates to the novel method for treating a patient that has osteoporosis. The patient may be having administered cyclase activating parathyroid hormone (CAP), commonly referred to simply as PTH, or CAP analogues.The patient receives an administration of a cyclase inhibiting parathyroid hormone peptide (CIP) having an amino acid sequence from between [(SEQ ID NO:1)] $PTH_{2-84}$ (SEQ ID NO:1) and [(SEQ ID NO:2)] $PTH_{34-84}$ (SEQ ID NO:3), preferably [(SEQ ID NO:3)] $PTH_{3-84}$ (SEQ ID NO:2) and [(SEQ ID NO:4)] $PTH_{28-84}$ (SEQ ID NO:8), or a conservatively substituted variant thereof exhibiting parathyroid hormone (PTH) antagonist activity in a therapeutically effective, but non-toxic amount that reduces the occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP. CIP also has the ability when administered alone to provide a therapeutic treatment for osteoporosis by means of the CAP rebound effect without hypercalcemia or osteosarcoma side effects. Administration can be either continuous or pulsatile, as in the administration of CAP.

The paragraph, beginning at page 5, line 3, has been amended as follows:

FIGURE 1 is a diagrammatic view of hPTH (SEQ ID NO:5).

The paragraph, beginning at page 5, line 20, has been amended as follows:

Preferred PTH antagonists of the present invention have an amino acid sequence from between $PTH_{2-84}$ (SEQ ID NO:1) and $PTH_{34-84}$ (SEQ ID NO:3) or a conservatively substituted

variant thereof exhibiting PTH antagonist activity, with the most preferred form being from between $PTH_{3-84}$ (SEQ ID NO:2) and $PTH_{28-84}$ (SEQ ID NO:8).

**In the Claims:**

Claim 1 has been amended as follows:

1. (Amended) A method for treating a patient that has osteoporosis and is being administered cyclase activating parathyroid hormone (CAP) or analogues thereof comprising also administering a cyclase inhibiting parathyroid hormone peptide (CIP) having amino acid sequence from between [(SEQ ID NO:1)] $PTH_{3-84}$ (SEQ ID NO:1) and [(SEQ ID NO:2)] $PTH_{34-84}$ (SEQ ID NO:3) or a conservatively substituted variant thereof exhibiting parathyroid hormone (PTH) antagonist activity in a therapeutically effective, but non-toxic amount that reduces the occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP.

Claim 2 has been amended as follows:

2. (Amended) The method of claim 1 wherein the peptide has an amino acid sequence from between [(SEQ ID NO:3)] $PTH_{3-84}$ (SEQ ID NO:2) and [(SEQ ID NO:4)] $PTH_{28-84}$ (SEQ ID NO:8).

Claim 5 has been amended as follows:

5. (Amended) A method for treating a patient that has osteoporosis comprising administering a cyclase inhibiting parathyroid hormone peptide (CIP) having amino acid sequence from between [(SEQ ID NO:1)] $PTH_{3-84}$ (SEQ ID NO:1) and [(SEQ ID NO:2)] $PTH_{34-84}$ (SEQ ID NO:3) or a conservatively substituted variant thereof exhibiting parathyroid hormone (PTH) antagonist activity in a therapeutically effective, but non-toxic amount that reduces the

occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP.

Claim 6 has been amended as follows:

6. (Amended) The method of claim 5 wherein the peptide has an amino acid sequence from between [(SEQ ID NO:3)] $PTH_{3-84}$ (SEQ ID NO:2) and [(SEQ ID NO:4)] $PTH_{28-84}$ (SEQ ID NO:8).